UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/390,634	09/07/99	PRICE	P 0942.4190002

HM22/0814
STERNE KESSLER GOLDSTEIN & FOX
1100 NEW YORK AVENUE N W
SUITE 600
WASHINGTON DC 20005-3934

EXAMINER	
KERR, J	
ART UNIT	**PAPER NUMBER**
1633	13

DATE MAILED: 08/14/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Advisory Action

Application No.	Applicant(s)
09/390,634	Price et al.
Examiner	**Art Unit**
Janet M. Kerr	1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED *Apr 23, 2001* FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.

b) ☐ In view of the early submission of the proposed reply (within two months as set forth in MPEP § 706.07 (f)), the period for reply expires on the mailing date of this Advisory Action, OR continues to run from the mailing date of the final rejection, whichever is later. In no event, however, will the statutory period for the reply expire later than SIX MONTHS from the mailing date of the final rejection.

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on *May 22, 2001*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will be entered upon the timely submission of a Notice of Appeal and Appeal Brief with requisite fees.

3. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search. (See NOTE below);

   (b) ☐ they raise the issue of new matter. (See NOTE below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

   NOTE: _____

4. ☒ Applicant's reply has overcome the following rejection(s):
   None, see attached.

5. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claim(s).

6. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because:
   See attached.

7. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

8. ☒ For purposes of Appeal, the status of the claim(s) is as follows (see attached written explanation, if any):
   Claim(s) allowed: *none*
   Claim(s) objected to: *none*
   Claim(s) rejected: *89-126*

9. ☐ The proposed drawing correction filed on _____ a) ☐ has b) ☐ has not been approved by the Examiner.

10. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

11. ☒ Other: *Interview summary attached.*

Deborah Clark
DEBORAH J. R. CLARK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Response to Arguments

Applicant's arguments filed 5/22/01 have been fully considered but they are not persuasive for the reasons of record and the reasons below.

It is argued that the specification provides sufficient guidance for one of skill in the art to make and use the claimed invention, that only routine experimentation is required to develop serum-free cell culture media that support the expansion of embryonic stem cells *in vitro*, and that obtaining embryonic stem cells from a variety of species was known in the art.

With regard to routine experimentation to develop serum-free cell culture media which support embryonic stem cell expansion *in vitro*, applicants rely on the teachings of Freshney, Gruber *et al.*, and Ham *et al.* to support the position that it is recognized in the art of cell culture that some degree of trial and error is routine in the development and optimization of media formulations and that while some experimentation is necessary, development and optimization of the media formulations in the instant invention do not require undue experimentation (see pages 2, and 11-14 of applicants' Response). This is not persuasive. The specification defines a defined medium formulation which comprises 38 components each having a specific concentration or, alternatively, having a concentration range spanning several orders of magnitude. While the specification has provided objective evidence that the formulation comprising 38 components is effective in supporting murine embryonic stem cell expansion *in vitro*, the specification provides no guidance with respect to which one or combination of the 38 components can be excluded from the formulation such that the resultant formulation is effective in not only supporting murine embryonic stem cell expansion *in vitro*, but also effective in supporting the expansion of all of the potential species of embryonic stem cells encompassed by the claimed invention. In this regard, the amount of experimentation required to formulate a medium composition which supports murine embryonic stem cell expansion, given the assumption that all 38 components are necessary, and not taking into account the minimum amount of each component required for expansion, or the maximum amount which can be tolerated by the embryonic stem cell without

causing toxicity, and assuming that only 2 of the 38 components are recited in the claim, using the formula:

$$nCr = \frac{n!}{r!\,(n-1)}$$

wherein n=36, and r=1 (i.e., n represents the number of remaining components to be tested, and 1 component is altered in the formulation), the number of possible combinations (c) of components to be tested for development and optimization of the medium formulation would be 6.8×10^{10}.

With regard to the embryonic stem cells *per se*, it is argued that exhibition of genetic information *in vivo* need not be a criterium in defining an embryonic stem cell. It is further urged that those of ordinary skill in the art regarded cells as embryonic stem cells by virtue of morphological characteristics, the ability to be maintained in culture in an undifferentiated state, and/or the ability to control the differentiation of the cells in culture. It is further argued that the prior art teaches embryonic stem cells from a variety of species as evidenced by the references supplied by applicants. Even if the claims were enabled with respect to putative embryonic stem cells from species taught in the prior art references, there is no objective evidence of record that the medium formulation, which is effective in supporting murine embryonic stem cell expansion *in vitro,* would be effective in supporting expansion of embryonic stem cells obtained from other species.

For the reasons of record, and the reasons above, the rejections are maintained.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet M. Kerr whose telephone number is (703) 305-4055. Should the examiner be unavailable, inquiries should be directed to Deborah Clark, Supervisory Primary Examiner of Art Unit 1633, at (703) 305-4051. Any administrative or procedural questions

should be directed to Kimberly Davis, Patent Analyst, at (703) 305-3015. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 305-7401.

Janet M. Kerr, Ph.D.
Patent Examiner
Group 1600